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Optically Active Isonitrile Ligand for Palladium-Catalyzed Enantioselective Bis-Silylation of Carbon-Carbon Double Bonds

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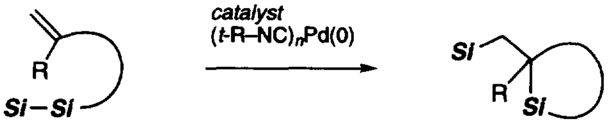
Abstract: Intramolecular bis-silylation of homoallylic alcohols proceeded enantioselectively in the presence of a catalyst prepared from Pd(acac)$_2$ and optically active isonitriles, derived from a common chiral source, (+)-ketopinic acid. © 1997, Elsevier Science Ltd. All rights reserved.

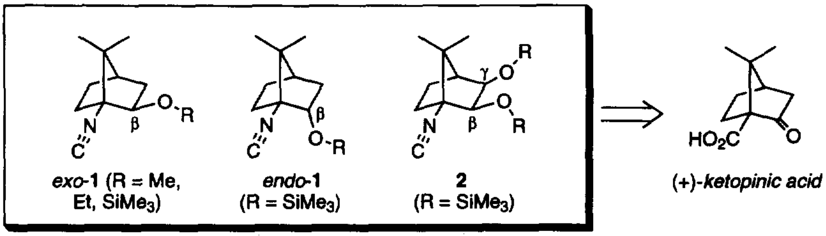
Recent advances in catalytic asymmetric synthesis have inevitably depended upon the development of chiral ligands for transition-metal complexes.[1] Although various chiral ligands containing phosphorus as well as nitrogen as the coordinating elements have been known, exploitation of a new class of chiral ligands is still highly desired for further development of efficient catalytic asymmetric reactions.

Isonitriles have been recognized as unique ligands for transition-metal complexes in view of the fact that they are isoelectronic with carbon monoxide and have various substituents at the nitrogen. A number of transition metal-isonitrile complexes have been synthesized and characterized.[2] Isonitriles, similarly to carbon monoxide, have also been utilized as a C_1 component in organic synthesis catalyzed by transition-metal complexes.[3] In general, isonitriles do not remain simply as ligands on transition metals in the synthetic reactions presumably due to their high reactivities.

A few years ago, we found that palladium(0)-*tert*-alkyl isocyanide complexes catalyzed the intra- and inter-molecular bis-silylation reaction of acetylenes; this was the first reaction employing a catalytic amount of isonitrile as the ligand on transition-metal complexes.[4] It has been mechanistically elucidated that the palladium(0)-*tert*-alkyl isocyanide complexes undergo the oxidative addition of disilanes to give the corresponding bis(organosilyl)palladium complexes, which react with carbon-carbon multiple bonds.[5] It is noteworthy that, unlike the conventional phosphine ligands, the *tert*-alkyl isocyanide ligand on palladium made also possible an intramolecular bis-silylation of olefins (eq 1).[6] Moreover, a finding that the stereoselective bis-silylation was markedly accelerated by an appropriate choice of the disilanyl group has broadened the synthetic scope of the reaction.[6c,7] Herein, we describe that optically active *tert*-alkyl isocyanides, employed as the ligands on palla-



(1)



Scheme 1. Optically active *t*-alkyl isocyanides employed for the enantioselective bis-silylation.

dium(0), induced intramolecular enantioselective bis-silylation of the carbon-carbon double bonds.

The optically active, chiral isonitriles employed in the enantioselective bis-silylation are listed in Scheme 1. We chose a rigid, bicyclic skeleton with a substituent *β* to the isocyano group, taking into consideration the linear structure of isonitriles, which might make it difficult to create an effective asymmetric environment in the vicinity of the metal center (Chart 1). Thus, *tert*-alkyl isocyanides *exo*-**1**, *endo*-**1**, and **2** were prepared from a common chiral source, (+)-ketopinic acid, through several steps including Curtius rearrangement and diastereoselective reduction of the carbonyl groups.[8,9]

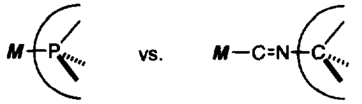
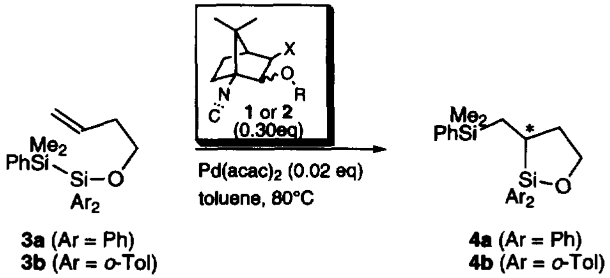


Chart 1. Effect of the steric environment of the ligand onto the metal center a phosphine complex (left) and an isonitrile complex (right).

A toluene solution of disilanyl ether **3a**, derived from 3-buten-1-ol and 1-chloro-2,2-dimethyl-1,1,2-triphenyldisilane, was stirred in the presence of a catalyst prepared from Pd(acac)$_2$ (2 mol%) and *exo*-**1a** (30 mol%) (Scheme 2). Unlike the reaction using achiral 1,1,3,3-tetramethylbutyl isocyanide, the reaction catalyzed by the *exo*-**1a**–palladium complex did not proceed at all at room temperature. Heating at 80°C for 2 h gave the five-membered product **4a** in good yield. After the removal of the palladium catalyst, the Si-C bond in the five-membered ring was selectively oxidized with retention of the configuration at the carbon atom to give diol **5** with 14%ee in 79% overall yield (eq 2; Table 1, entry 1).[6,10,11] The absolute configuration of **4** was

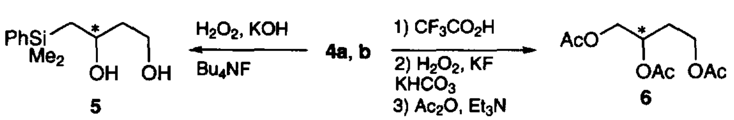


Scheme 2

Table 1. Palladium-catalyzed enantioselective bis-silylation of carbon-carbon double bonds in the presence of chiral isonitriles

entry	substrate (Ar)	isonitrile (R)	%yield of 5[a]	%ee[b] (config)
1	**3a** (Ph)	*exo*-**1a** (Me)	79	14 (*S*)
2	**3a**	*exo*-**1b** (Et)	85	20 (*S*)
3	**3a**	*exo*-**1c** ($SiMe_3$)	83	33 (*S*)
4	**3a**	*endo*-**1c** ($SiMe_3$)	76	7 (*R*)
5	**3b** (*o*-Tol)	*exo*-**1c**	74	55 (*S*)
6	**3b**	**2** ($SiMe_3$)	87[c]	64 (*S*)

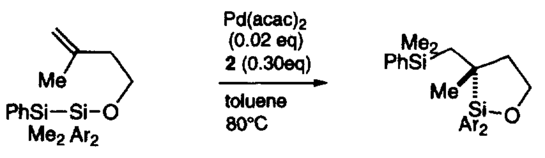
[a] Isolated yield. [b] Determined by HPLC after the transformation into diol **5** by H_2O_2 oxidation in the presence of TBAF and KOH. [c] Yield of **4b**.



(2)

determined by the optical rotation of 1,2,4-butanetriol triacetate **6**,[12] which was obtained by acidic cleavage of the Si-Ph bond of **4** followed by oxidation and acetylation (eq 2). The significant improvement of enantioselectivity achieved by use of *exo*-**1b** and **c** with the larger substituent R (entries 2 and 3) suggests that an appropriately bulky *exo*-substituent at the β-position of the isonitrile **1** is crucial to attain high stereoselectivity. On the other hand, diastereomeric *endo*-**1c** induced the reverse enantioface selection to give the (*R*)-product with low enantiomeric excess (entry 4). The substituents on the disilanyl group of the starting **3** also affected the enantioselectivity. Thus, the disilanyl ether **3b** with *o*-tolyl groups at the silicon atom proximal to the oxygen atom gave better selectivity than that for **3a** (entry 5). Consequently, isonitrile ligands **2**, in which the β-*exo*-substituent effect may be reinforced by the "buttressing effect"[13] of the γ-*exo*-substituent, significantly improved the enantioselectivity in the bis-silylation of **3b** (entry 6).

Finally, it was found that intramolecular bis-silylation of disilanyl ether **7** derived from 3-methyl-3-buten-1-ol proceeded with 78%ee in the presence of **2** to give five-membered **8** with a chiral *tert*-alkyl-silicon bond (eq 3).[14] The optically active **8** could be transformed to 2-methyl-1,2,4-butanetriol in high yield by the oxidation procedure described above.[15]



7 (Ar = *o*-Tol)

(*S*)-**8** (59%; 78%ee)

(3)

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